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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/147,947	03/24/1999	NOBUO TSURUOKA	001560-349	2472

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EXAMINER

MOORE, WILLIAM W

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/147,947

Applicant(s)

TSURUOKA ET AL.

Examiner

William W. Moore

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5,7-9,14-16,21-26,31-33,37-39,44-46,51 and 63 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 5,7-9,14,21,22,31,37 and 44 is/are allowed.
- 6) ☒ Claim(s) 15,16,23-26,32,33,38,39,45,46,51 and 63 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: ____.

DETAILED ACTION

Response to Amendment

Applicant's amendment after final rejection filed December 1, 2003, was entered and claims 6, 12, 40, 47, and 60-62 were canceled at Applicant's request. Applicant also filed a Notice of Appeal on December 1, 2003. Applicant would ordinarily have received an indication of allowance of claims because only claims 6, 12, 40, 47, and 60-62 had been subject to rejection and were cancelled and the other claims pending herein had been indicated as allowable in the Office communication mailed May 29, 2003. However, rejections that should have been made of claims 15, 16, 23-26, 32, 33, 45, 46, 51, and 63 had not been made in the Office communication mailed May 29, 2003, and this action is not made final because new grounds of rejection are stated herein. Claims 5, 7-9, 14, 21, 22, 31, 37 and 44 remain allowable in their present form and the subject matters now stated by claims 15, 16, 23, 24, 32, 33, 38, 39, 45, and 46 may be included in allowable claims if claims 15, 16, 23, 24, 32, 33, 38, 39, 45, and 46 are amended so that a polypeptide consists of the entire serine protease domain, which has utility, as well the remaining positions of the amino acid sequence of SEQ ID NO:2 that extend amino-proximally to the boundary of the kringle domain, position 40, or to the boundary of any of the scavenger receptor cysteine-rich domains, i.e., position 117, position 227, or position 547. The subject matters now stated by claims 25, 26, 51, and 63 may be included in allowable claims by amending these claims to overcome the rejection for lack of utility under the first paragraph of 35 U.S.C. § 112 stated below by removing the term, "or activating", and adding a critical component of any claimed process, the specific substrate disclosed at line 12 of page 26 of the specification, and also by amending these claims to overcome the rejection for indefinite description under the second paragraph of 35 U.S.C. § 112 stated below.

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Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 15, 16, 23, 24, 32, 33, 38, 39, 45 and 46 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility.

This is a new ground of rejection of the claims listed above, thus this communication is not made final. A claimed invention must possess a specific, substantial and credible *in vitro* or *in vivo* utility, but the instant application cannot identify any specific, substantial, utility for an isolated polypeptide that consists only of the kringle domain described by claim 23 or for an isolated polypeptide that consists only of either of the scavenger receptor cysteine-rich domains described by claim 24. It is agreed that the specification demonstrates that isolated polypeptides consisting of the integral protease of SEQ ID NO:2 herein, or consisting of the protease domain from position 578 through position 822, inclusive, of SEQ ID NO:2 herein, have a specific and substantial utility in cleaving a definite substrate disclosed at page 26, line 12, of the specification. The specification provides no evidence, however, that an invention that consists of the kringle domain of claim 23, or that consists of either of the scavenger receptor cysteine-rich domains of claim 24, had a specific utility known to the inventors at the time the application was filed. Claims 15, 16, 32, 33, 38, 39, 45 and 46 lack utility because the expression vectors and cells comprising the expression vectors, as well as recombinant methods of making the encoded domains, can provide no product having a specific utility. While the specification proposes, at pages 7 and 8, potential diagnostic and prognostic uses for a claimed nucleic acid sequence of, e.g., claims 15 and 16, these are not specific because there is no disclosure of what disease state or medical condition may or may not be diagnosed. A method of use of a material for further

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research to determine, e.g., its specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). Mere allegations of a prospective, potential, utility cannot rise to the level of a credible assertion of a specific *in vivo* utility that is substantial. Indeed, the specification's diffuse assertions indicate the contrary, that Applicant knew no specific utility for the domains of claims 23 and 24 encoded by nucleic acid sequences of claims 15 and 16 at the time the application was filed that would permit an immediate use by the public of a disclosed nucleic acid sequence, or any use by the public of an expression vector or cell comprising a disclosed nucleic acid sequence, or a method of making these domains.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 16, 23, 24, 32, 33, 38, 39, 45 and 46 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 25, 26, 51 and 63 are rejected under 35 U.S.C. § 112, first paragraph, because the specification is not enabling either for

1) any assay method to detect activators of a disclosed serine protease, whether the assay measures binding affinity or measures the rate of cleavage of the substrate disclosed at page 26, line 12, of the specification, or,

2) assay methods to detect inhibitors of a disclosed serine protease unless a decrease in the rate of cleavage of the substrate disclosed at page 26, line 12, of the specification is measured, whether or not binding affinity is also measured.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, make and use the invention commensurate in scope with these claims.

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This is a new ground of rejection of the claims listed above, based in part on the absence of a teaching of any class of compounds that may be suspected to be serine protease activators, thus this communication is not made final. Claims 23-26, 51 and 63 contemplate processes, such as assays, for screening or detecting "physiologically active substances" that activate the serine protease consisting of the integral amino acid sequence of SEQ ID NO:2 or its protease domain consisting of the sequence from position 578 through position 822, inclusive, of SEQ ID NO:2 herein. While the prior art of record discloses several classes of compounds known to be inhibitors of serine protease activity, permitting the artisan to practice an assay to detect an inhibitor that measures a decrease in the rate of cleavage of the substrate disclosed at line 12 of page 16 of the specification, neither the specification nor the prior art teaches or suggests how to choose any class of compounds that might be screened for activation of the proteolytic activity of any serine protease. Furthermore, neither the specification nor the prior art suggests how a compound that might bind a serine protease with any affinity may be assayed for an ancillary inhibitory activity unless a decrease in the rate of cleavage of a recognized substrate for the protease is measured.

It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (recognizing and applying the "*Forman*" factors). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors relevant to analysis of enablement). Applying the "*Forman*" factors discussed in *Wands, supra*, to Applicant's disclosure, it is apparent that:

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- a) the specification lacks adequate, specific, guidance for selecting any class of compounds from which an activator of serine protease activity might be drawn or any way to measure protease inhibition other than by measuring the rate of decrease of cleavage of a single, disclosed, substrate,
- b) the specification lacks working examples wherein an activator is drawn from any class of compounds known to activate of serine protease activity, as none are known yet in the art, for assay in a process of screening for or identification of an activator, and lacks working examples wherein binding affinity or inhibition is measured by any process other than measuring the rate of decrease in the cleavage of the single disclosed substrate,
- c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such processes of screening for, or identification of, any serine protease activator, and,
- d) unpredictability exists in the art where no class of compounds has yet been identified that activates any serine protease.

Thus the scope of processes embraced by "activating activity" and the conjunction of the phrases "inhibitory activity" and "binding affinity", is unsupported by the present specification even if taken in combination with teachings available in the prior art.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25, 26, 51 and 63 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25 and 51 are indefinite in their recitations, "screening physiologically active substances", because the artisan cannot determine their metes and bounds by reading the claims, even in light of the specification, to determine what "physiological activity" may be "screened" other than inhibition of protease activity, whether or not binding affinity is measured. Claims 25 and 51 are also indefinite because, even though they recite "comprising the steps of", they state only a single step, measuring, but do not provide for the common presence of a protease, candidate inhibitor, and something to be measured such as the substrate disclosed at page 26, line 12, of the specification, in any step of a process and because they fail to describe how to measure binding affinity by determining a measurable activity. Claims 26 and 63 are similarly indefinite in failing

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to provide for common presence in any step of a process of a protease, candidate inhibitor, and something to be measured such as the substrate disclosed at page 26, line 12, of the specification.


Claims 25, 26, 51 and 63 are further indefinite because they are incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: detection of inhibition or activation as measured by a decrease or an increase in the rate of cleavage of the substrate disclosed at page 26, line 12, of the specification in the presence of a candidate inhibitor or activator relative to the rate of cleavage in the absence of any candidate inhibitor or activator.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is now 571.272.0933. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can now be reached at 571.272.0928. The fax phone numbers for all communications for the organization where this application or proceeding is assigned remains 703.872.9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is now 571.272.1600.

William W. Moore
April 26, 2004


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